Dynamics of vesicular nanotubulation

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Dynamics of vesicular nanotubulation

(with G. Ananthakrishna, Materials Research Centre, IISc, Bangalore)

- B. Ashok & G. Ananthakrishna. Dynamics of vesicle pulling. *Proceedings of the Fourth National Conference on Nonlinear Systems & Dynamics, NCNSD-2008*, 72 (2008).

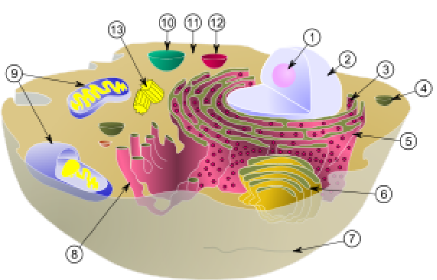
- B. Ashok & G. Ananthakrishna. Dynamics of vesicular nanotubulation. (2009 / 2010) .

1. **Vesicles & their nanotubulation**

2. **The Motivation for doing this work**

3. **Comparison with results from experiments**

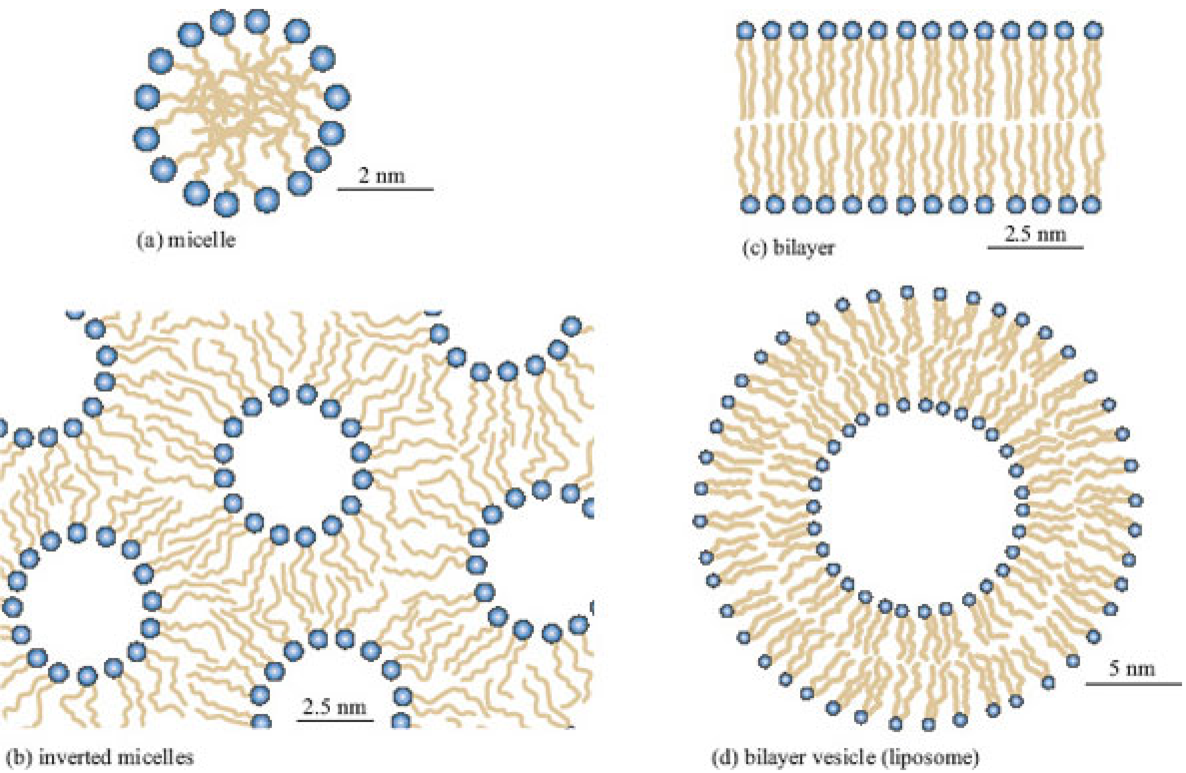
4. **Applications of this work**

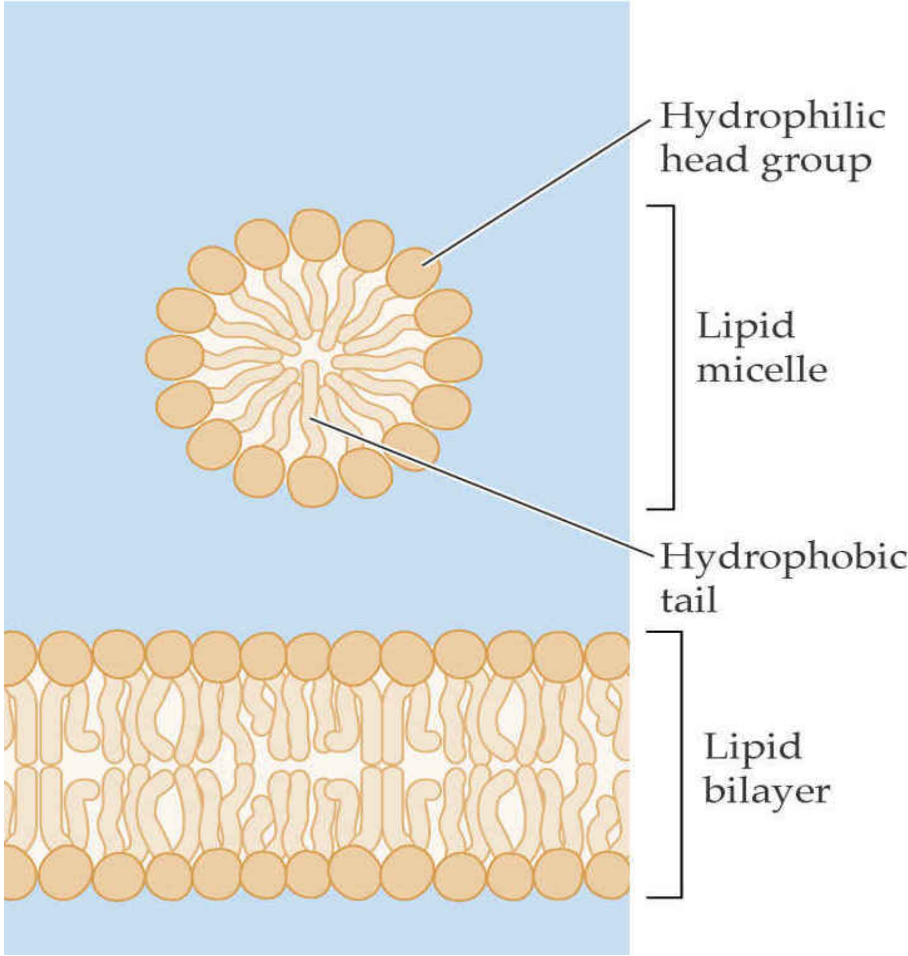


Vesicles, Micelles

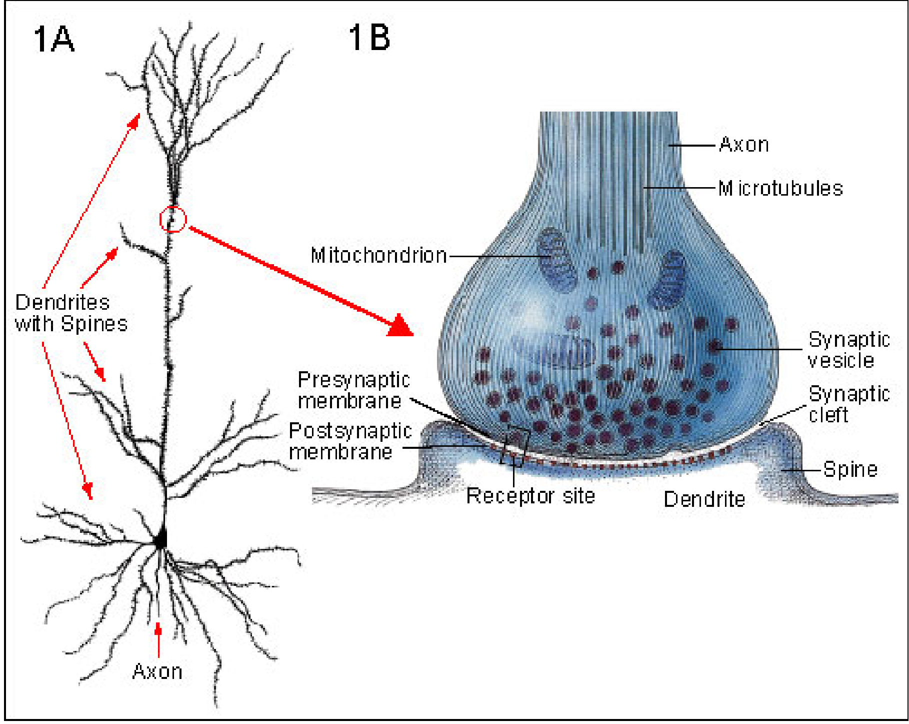
B. Ashok & M. Muthukumar, Rheology of wormlike micelles (2009)

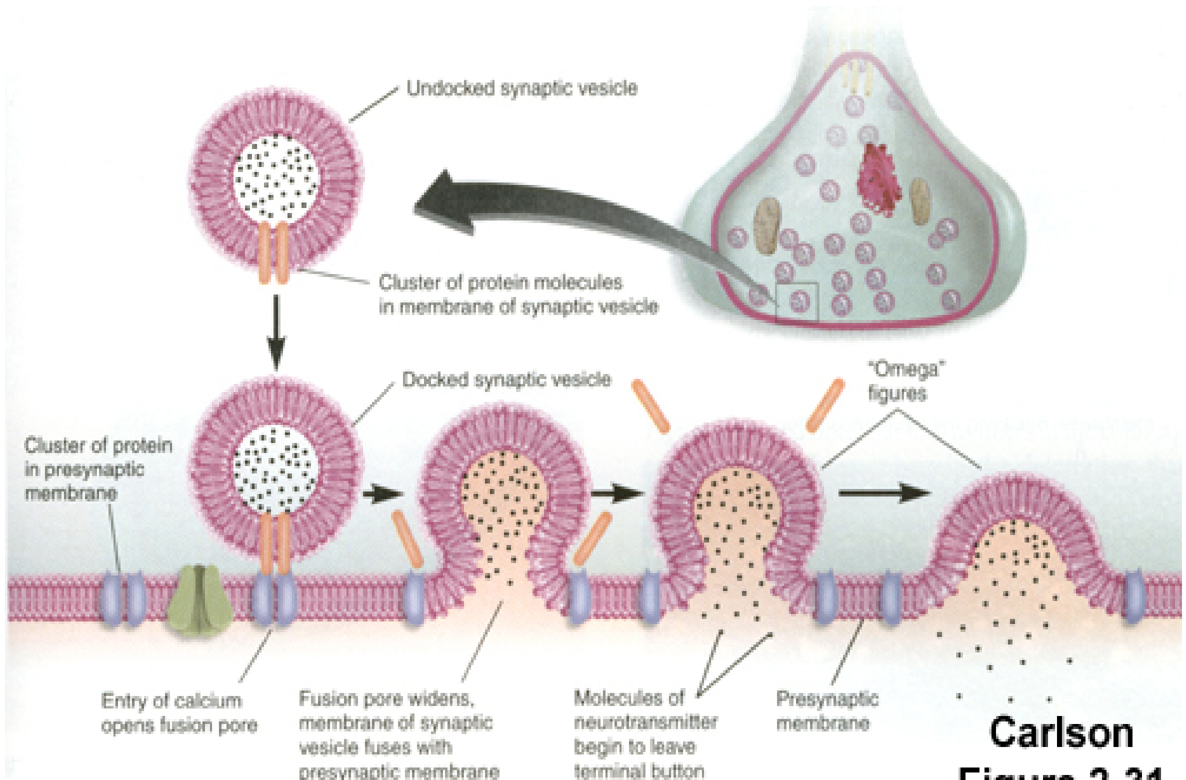
Lipid molecules form various structures -- vesicles, micelles, bilayer structures, liposomes, membranes, etc.





Fluctuations in neurotransmitter levels at synapses are an important source of neuronal noise affecting neuronal firing activity.





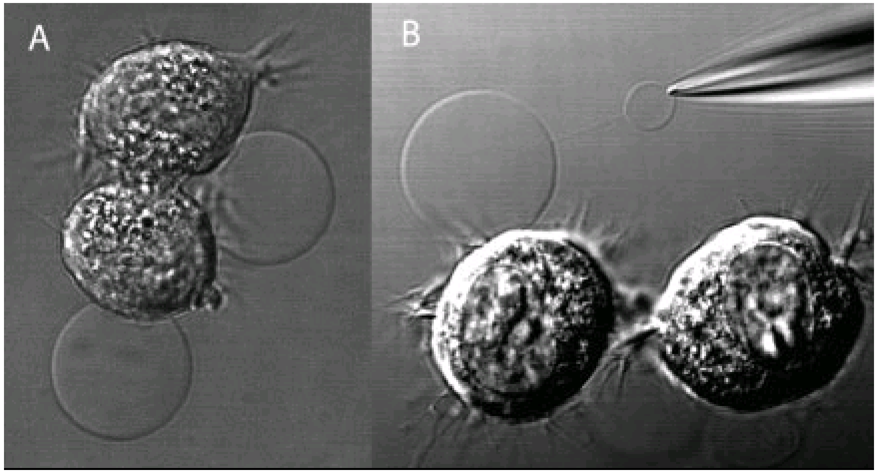
Carlson Figure 2-31

Noise plays an important role in synchronizing activity between coupled neurons

N. Malik, **B. Ashok** & J. Balakrishnan, *Eur. Phys. J. B* **74**, 177 (2010).

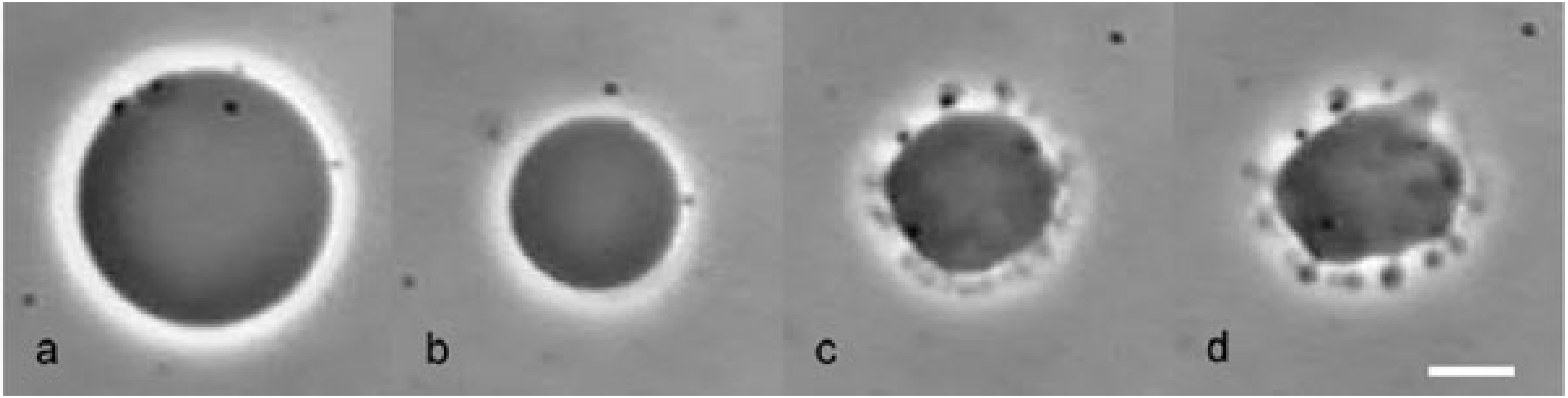
N. Malik, **B. Ashok** & J. Balakrishnan, *Pramana: journal of physics* **74**, 189 (2010).

Image clearly showing vesicles and tube formation



(A) DIC image of adherent NG108-15 cells, displaying membrane blebs induced by a combination of DTT and formaldehyde. (B) Subsequently, one bleb was electroinjected with a buffer-filled micropipet. Following translation of the micropipet, a nanotube connection is formed. Buffer injection leads to the formation of a daughter vesicle at the micropipet tip. (Reprinted with permission from the American Chemical Society)

Shape instabilities can arise during tube formation

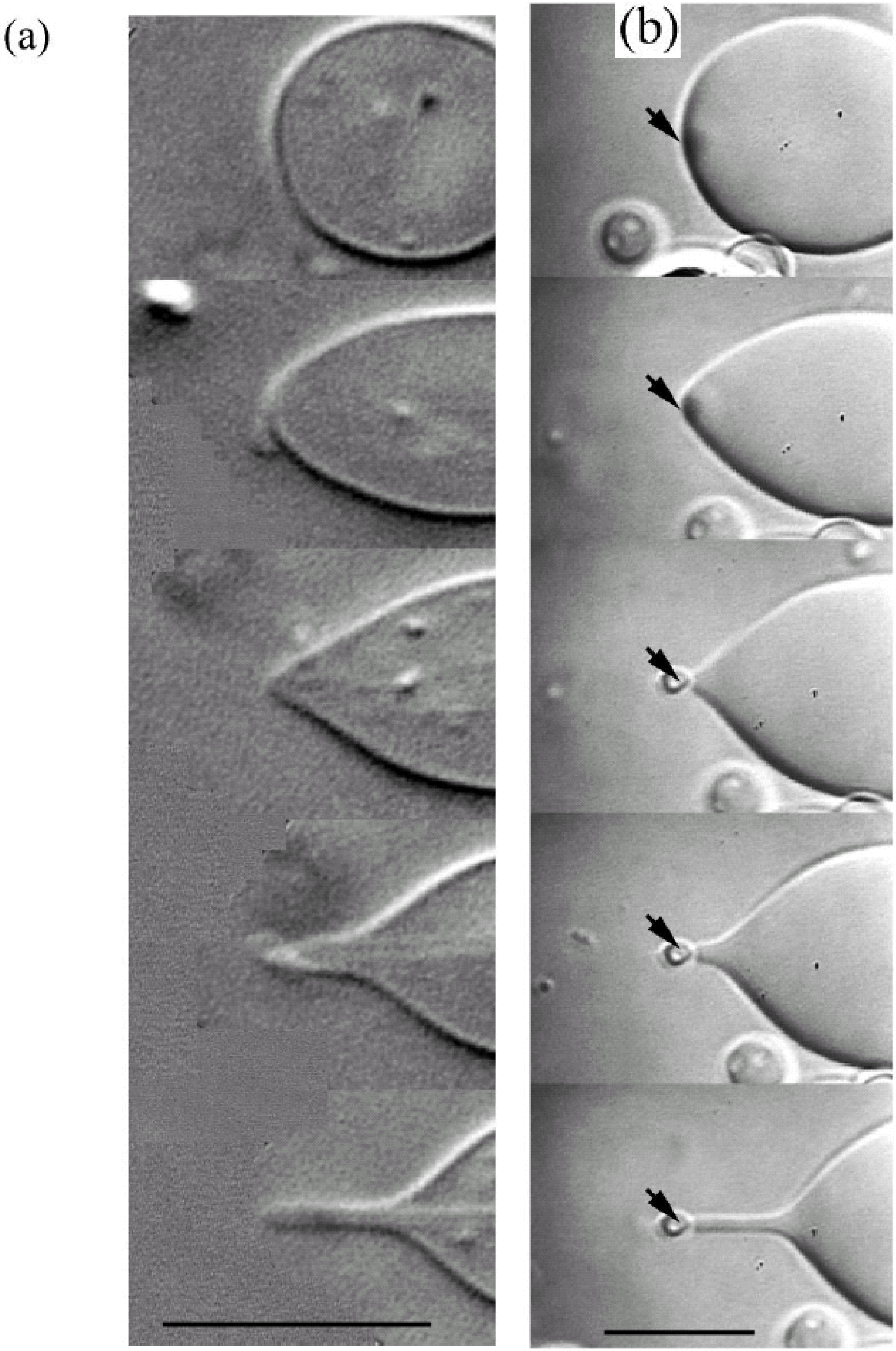


Transformation of the shape of a negatively charged giant vesicle (10%) in contact with positive small vesicles (1%). After a pore opening (b), the apparent diameter of the vesicle decreases. Instabilities grow around the vesicle, probably due to the aggregation of SUVs and to the fast increase of the surface excess which follows as a consequence (bar: 10 μm).

Instabilities during pulling of vesicles

(from P. Bassereau, et al., Instituut Curie, Paris)

Pulling of a vesicle by an optical tweezer



From Fygenson, Marko & Libchaber,
Phys. Rev. Lett. **79**, 4497 (1997).

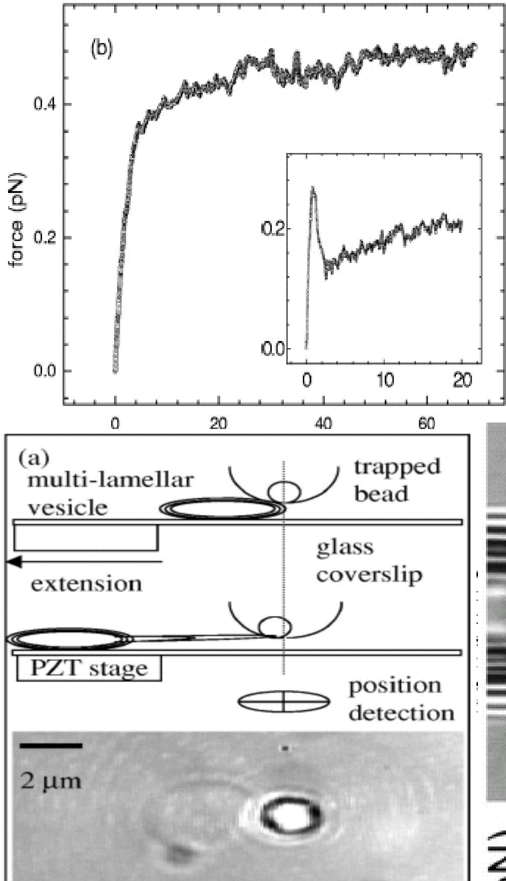
Mechanics of Microtubule-Based Membrane Extension

FIG. 2. (a) Closeup of a membrane extension generated by several growing microtubules encapsulated within a vesicle. Scale bar: 10 μm. (b) A membrane extension drawn from a fluctuating vesicle using optical tweezers (830 nm single-mode diode, 200 mW). Scale bar: 10 μm. Arrowhead indicates the location of the tweezer. The vesicle is in an osmotically matched NaCl solution which creates a large refractive index mismatch with the interior for better contrast and easier tweezing. The diameter of the extension is ~1 μm.

Force vs extension plots

(Constant pulling velocity v)

From: Roopa & Shivashankar, *Appl. Phys. Lett*. 82, 1631 (2003)



From Cuvelier, *et al*., *Europhys. Lett*. **71**, 1015 (2005).

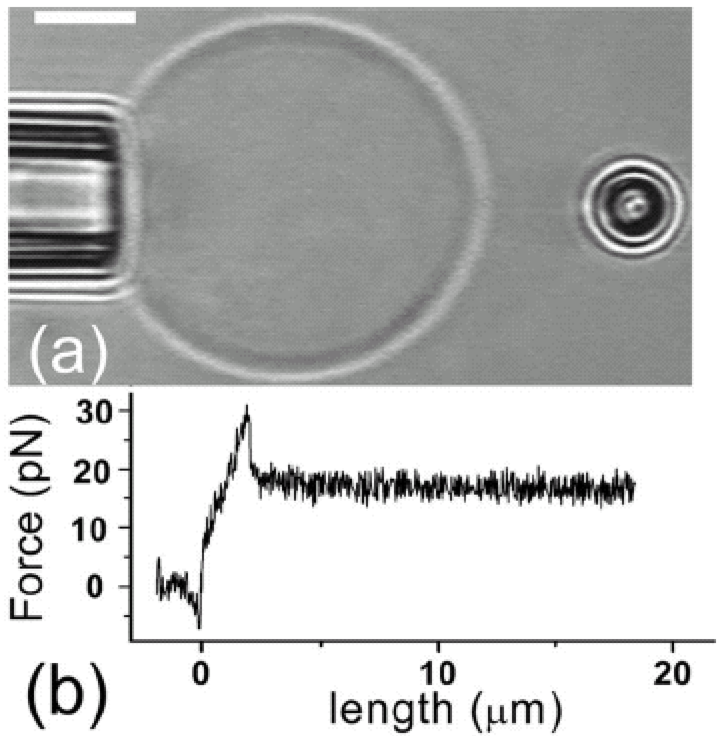


Fig. 1

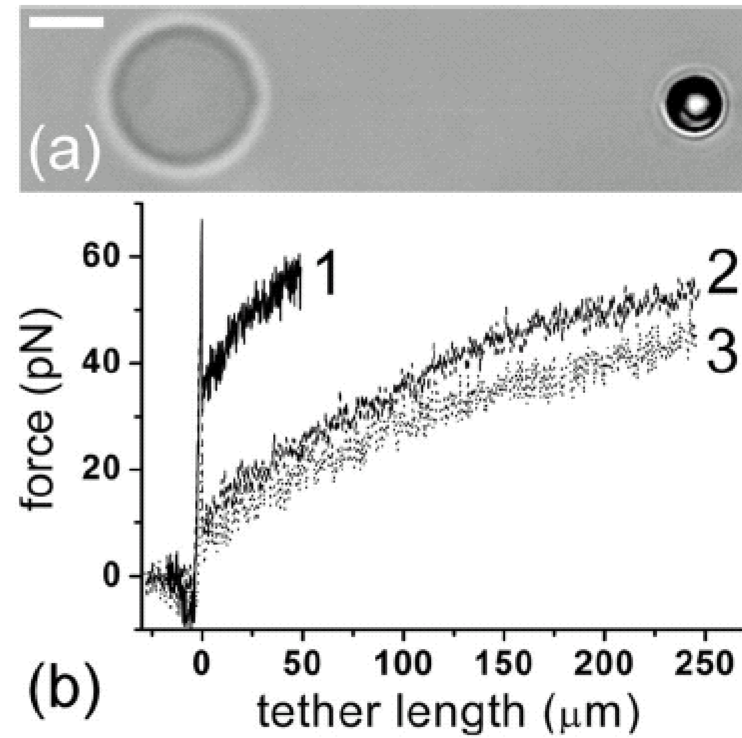


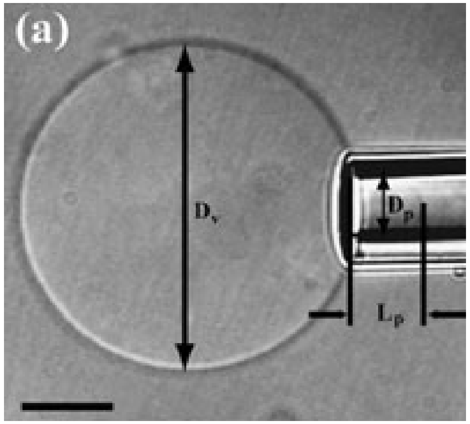
Fig. 2

No satisfactory theory yet that explains all features of the curve including serrations.

Fig. 1 – (a) Micrograph of the tether extraction experiment at constant membrane tension (set by micropipette aspiration). Scale bar $5\,\mu$m. (b) Tether force *vs.* extension as measured by optical tweezers. $\sigma = 0.06\,\mathrm{mN/m}$ and $\kappa = 12 k_{\mathrm{B}}T$.

Fig. 2 – (a) Micrograph of the tether extraction experiment when vesicles are adhered to the substrate. Scale bar $5\,\mu$m. (b) Representative force-extension curves for different vesicles (radii 7.7, 11.5 and $13.5\,\mu$m).

Dynamics of vesicular nanotubulation



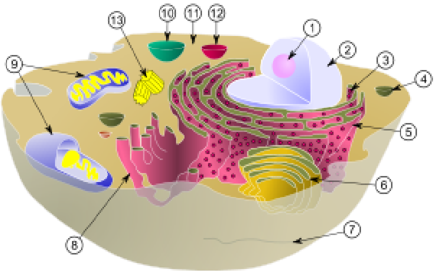
The Motivation

Why are we interested in this?

Vesicles form an integral part of cell transport mechanisms.

Theoretical studies of nanotubulation – no definitive explanation for all experimental observations

Can be used for nanotube creation; of use in nanotube-and-container networks which might be employed for drug-delivery etc.



Theory for dynamical behaviour had not been addressed so far

Experimental observations in the Force-Extension curve that we should be able to reproduce through our theory:

- Sharp rise in magnitude
- Sudden drop
- Plateau like-behaviour, accompanied with serrations

Other groups who have worked on the problem include:

- Evans & collaborators (U. Br.Columbia & Boston U.),
- Hochmuth & collaborators (Duke U.)
- Borghi, Brochard-Wyart, Cuvelier, Rossier (Institut Curie),
- Tom Powers (Brown Univ.)
- Greg Huber (Boston /U.Conn.)
- Ray Goldstein (U. of Cambridge & U. Arizona)

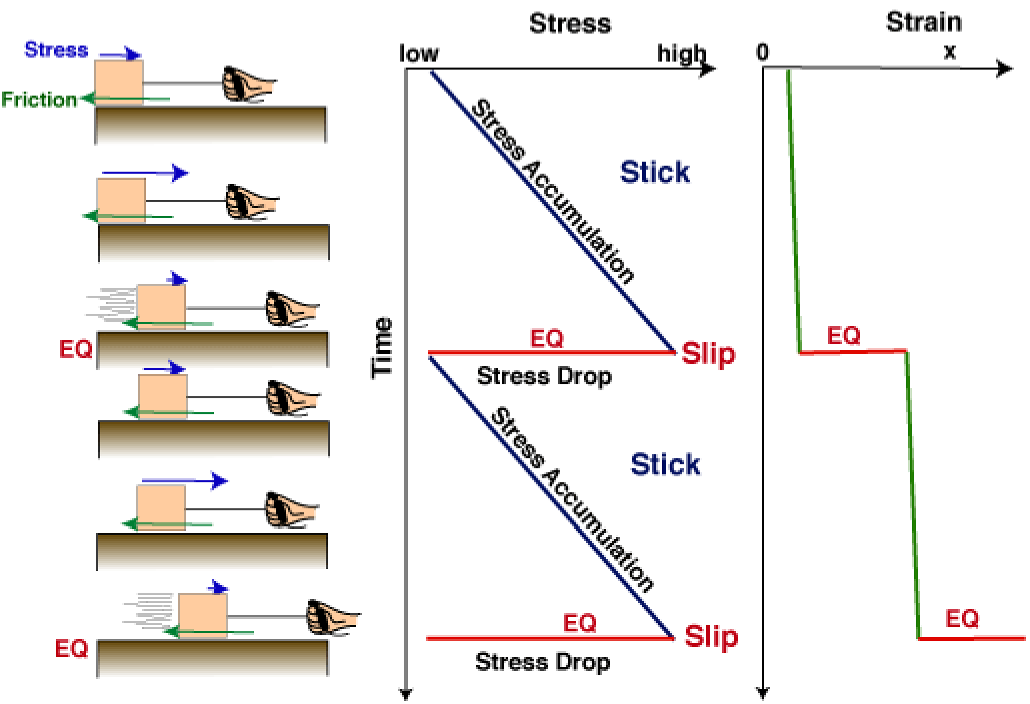
None of the theory satisfactorily addresses all the issues,

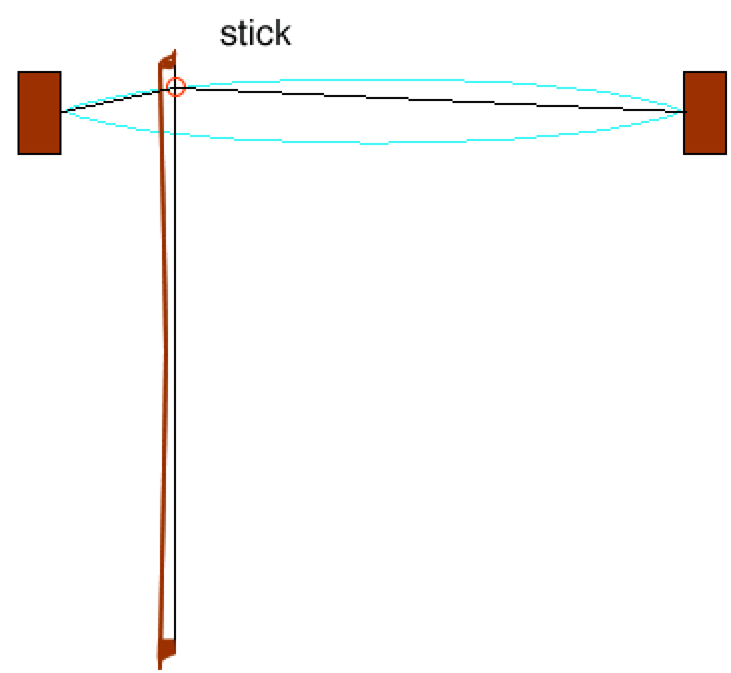
Dynamic behaviour NOT treated.

Stick-slip phenomena

Earthquake

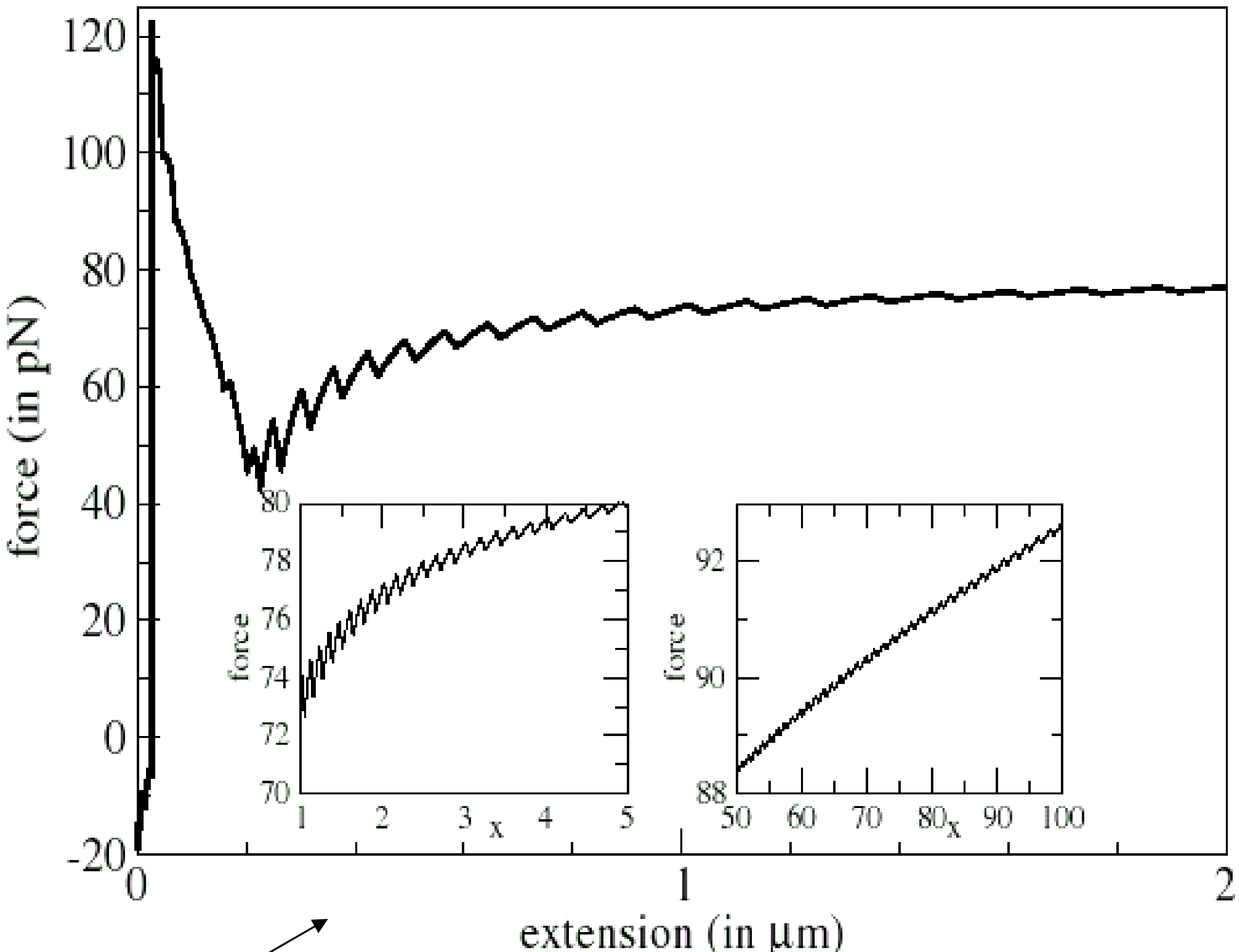
Violin bow & string

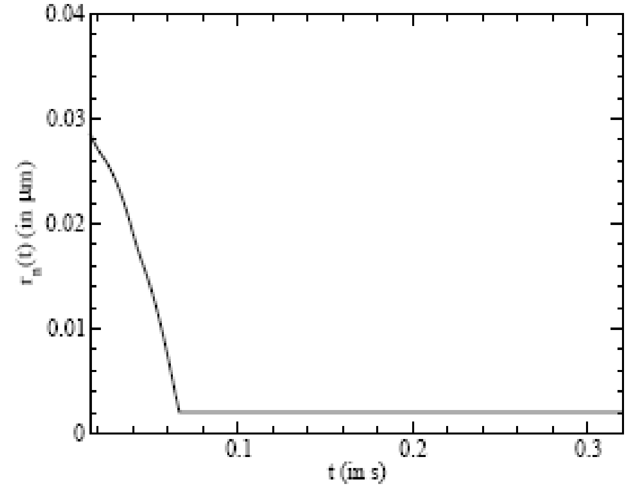




(Image sources (L): quakeinfo.ucsd.edu/~gabi/sio15/   (R): www.phys.unsw.edu.au/jw/torsional.html)

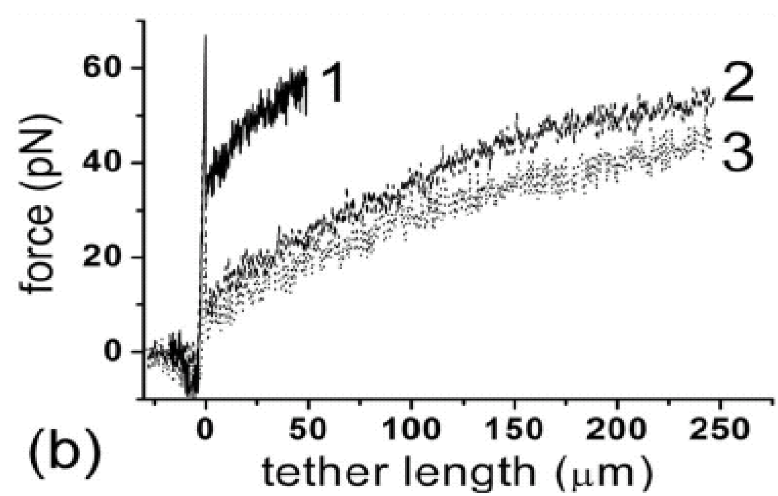
We account for stick-slip phenomena and vesicular deformation, dissipative effects due to the fluid to obtain a final expression for the forces acting on the vesicle



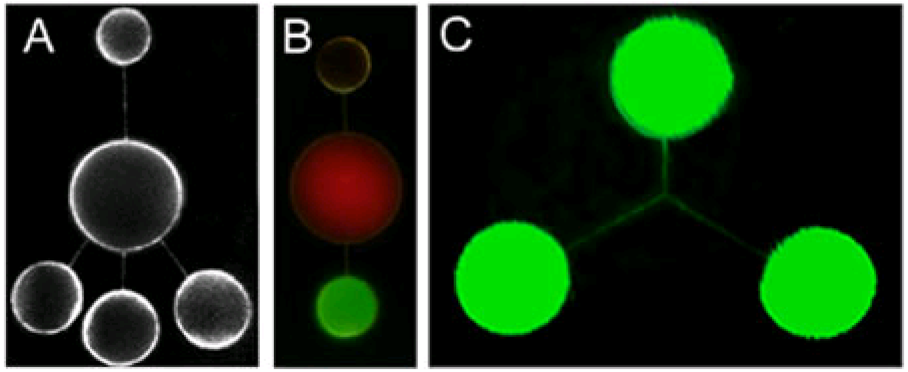


<u>Our results</u> are in qualitative agreement with the behaviour seen experimentally.

From Cuvelier, *et al.*,
Europhys. Lett. **71**, 1015 (2005).



(b)



Networks of nanotubes and containers formed using mechanical excitation. The nanotubes are between 100 and 200 nm in radius and the containers 4-10 μm in diameter. A shows an open, five-liposome network stained with a fluorescent membrane dye. In B, the contents of the three nanotube-connected liposomes have been differentiated using fluorescent dyes and fluorescent colloidal particles. C shows a three-way nanotube junction. (Image: Orwar Research Group)

CONCLUSIONS

We are able to get qualitative agreement with experimental observations:

Serrations are shown to arise from inherent nonlinearities & frictional effects

We get all of the following observed behaviour in the force-extension plot:

- **Initial serrations**
- **Sharp rise in magnitude**
- **Sudden drop**
- **Plateau like-behaviour,   accompanied with serrations**
- **Gently rising plateau**

Hence a proper understanding of the process will give us the ability for manipulating vesicles & making nanotubules –useful for construction of nanofluidic devices, or very specific drug delivery applications